

REMARKS

Applicants respectfully request reconsideration of the present application for the reasons that follow.

Examiner Interview Summary

Applicants thank the Examiner for courtesies extended in a telephonic interview with Applicants' representatives Heather Gerard, inventor Michael Slater, and attorney Lynda Fitzpatrick on December 23, 2010 ("the telephone interview"). During the telephone interview, the outstanding obviousness rejections were discussed. The Examiner indicated that certain arguments and amendments to the claims may result in the withdrawal of the rejections. Such arguments and amendments have been put forth below. Applicants appreciate the Examiner's time and attention to these matters.

Status of the Claims

With entry of this amendment, claims 1, 3, 4, 6, 7, 9-13, 36, 84, 85, and 87-111 are pending in the present application. Claims 2, 5, 8, 14-35, 37-83 and 86 are canceled. Applicants have amended claims 1, 84, 85, 100, and 101 for clarity. The amendments add no new matter.

Claims Rejected Under 35 U.S.C. §103(a)

Claims 1, 3, 4, 6, 7, 9, 10, 36, 84-109 were rejected under 35 U.S.C. § 103(a) as being obvious over five references, namely U.S. Patent No. 6,096,523 issued to Parrott et al. ("Parrott"); U.S. Patent Publication No. 2004/0166567 to Santi et al. ("Santi"); Berg, et al. (1996) *Escherichia coli* and *Salmonella*, Neidhardt, Vol. 2, pp. 2588-2612 ("Berg"); U.S. Patent No. 5,811,093 issued to Merrill et al. ("Merrill"); and Holt (<http://wheat.pw.usda.gov/~laso/methods/donis/plasmid/plsmid10.html>).

Claims 1, 3, 4, 6, 7, 9-13, 36, 84-109 were rejected under 35 U.S.C. § 103(a) as being obvious over Parrott in view of Santi, Berg, Merrill, and Holt and further in view of U.S. Patent Publication No. 20010029027 to Innerarity et al. ("Innerarity").

Claims 1, 3, 4, 6, 7, 9-13, 36, 84-111 were rejected under 35 U.S.C. 103(a) as being obvious over Parrott in view of Santi, Berg, Merrill, Holt, and Innerarity and further in view of U.S. Patent No. 6,709,861 issued to Mead et al. ("Mead").

Applicants respectfully traverse the rejections as set forth below.

Independent Claim 1

The Examiner alleges that the numerous references cited above combine to teach every element of claim 1, concluding that “each of these elements is known in the art.” See Final Action of 10/28/2010 (“Final Action”) at 5-7. Applicants respectfully submit that the present rejections under § 103(a) should be withdrawn because one of skill in the art would not have been motivated to combine the teachings of all five distinct cited references and because the cited references, even if combined, do not teach or suggest every element of claim 1.

First, a person of skill in the art would not have been motivated to combine Parrott, Santi, Berg, Merrill, and Holt—a total of five distinct references—to derive the subject matter of claim 1. In fact, in view of the sea of available technical references and information available at the time of the invention, there would have been no reason for one of skill in the art to particularly select these five references, let alone the specific, narrow aspects of each individual reference relied upon by the Examiner. The Examiner’s alleged *prima facie* case relies upon impermissible hindsight, starting from the claimed invention and attempting to support an obviousness rejection by cherry-picking isolated passages from a vast array of cited references. No actual person of skill in the art would have had any motivation to assemble the particular aspects of the myriad cited references at the time the invention was made. Therefore, applicants respectfully submit that the present rejection lacks adequate support and should be withdrawn.

Moreover, even, assuming *arguendo*, that the cited references were combined, they still do not teach or suggest each element of claim 1. At the time of the invention, canonical cloning techniques included time-consuming intermediate steps necessary to remove unwanted enzymes and purify the DNA fragments of interest between the restriction and ligation steps. See Specification at ¶ 7. As amended, claim 1 teaches a method for directional subcloning of DNA fragments that permits ligating DNA fragments derived from the first and second vectors directly, without intervening purification steps following endonuclease treatment. In other words, the claimed method teaches ligation in the presence of one or more restriction enzymes and all four linear DNA fragments—not only the first linear DNA fragment (comprising the DNA sequence of interest) and third linear DNA fragment (comprising the vector having the second selectable marker) that make up the finished third vector, but also the discarded second and fourth linear DNA fragments. Whether the first vector, the second vector, or both enter step (c) uncut, the one or more restriction enzymes ensure that all four linear DNA fragments will be produced. Thus, the DNA ligase and one or more restriction enzymes used in the claimed method catalyze the cleavage and ligation reactions necessary to produce the third vector, all in

the same mixture without intervening steps to remove restriction enzymes or purify the desired linear DNA fragments. The claimed method is thus highly efficient, offering substantial savings in cloning time and effort.

Futhermore, the claimed method is not taught by any of the cited references. The cited references in fact specify a time-consuming, stepwise cloning procedure by which (1) each vector is separately digested with restriction enzymes, (2) the linear DNA fragments from each digested vector are electrophoretically separated, (3) the linear DNA fragments of interest are excised from the gel, (4) the excised DNA fragments are purified, and (5) the purified DNA fragments are combined in a ligation reaction.

Holt teaches a sequential procedure with separate “Plasmid Vector Preparation,” “Insert Preparation,” and “Ligation Reaction” stages. Holt at 3-5. Among its overarching materials and methods, Parrott teaches that “DNA fragments were purified from gels” for use in its ligation and cloning procedures. Parrott at col. 10, line 10. Similarly, Santi teaches performing ligation reactions using isolated fragments of interest that have been endonucleolytically cleaved from donor vectors. Santi at Figs. 3A, 3B, and 5. Merrill describes its cloning methods with scant detail, referring only to standard laboratory manuals and “techniques known in the art” with no indication of the unconventional, streamlined cloning approach used the present application. Merill at col. 13, line 29 and col. 17 line 65 – col. 18, line 3. Berg is a review article that does not provide specific detail regarding any cloning methods, much less a teaching of suggestion of the claimed method. Thus, none of the cited references teaches or suggests cloning without purifying restriction fragments. Moreover, Holt teaches that, without the traditional, laborious purification steps, successful cloning is “virtually impossible.” Holt at 2. Thus, the cited references not only fail to disclose the claimed cloning method but also actively teach away from such a strategy.

In view of the foregoing, applicants respectfully submit that independent claim 1 is allowable. Reconsideration and allowance of claim 1 is respectfully requested.

Independent Claim 85

As amended, independent claim 85 comprises the same or similar elements discussed above regarding claim 1. Accordingly, applicants respectfully submit that claim 85 is allowable for at least the reasons above. Reconsideration and allowance of claim 85 is respectfully requested.

Dependent Claims 3, 4, 6, 7, 9, 10-13, 36, 84, and 87-111

Claims 3, 4, 6, 7, 9, 10-13, 36, 84, and 87-111 depend directly or indirectly from independent claims 1 or 85 and are therefore allowable for at least the reasons discussed above. Allowance of these claims is respectfully requested.

Dependent Claims 6, 7, 9, 84, 89-92, 103, 104, and 106-109

The Examiner further alleges that Parrott teaches “any two rare restriction sites may be used in the first and second vector, including different ones.” Final Action at 3. Parrott, however, explicitly limits its disclosure to rare cutter restriction sites of at least 9 bp in length. Parrott, col. 5, lines 28-35. Claims 6, 7, 9, 84, 89-92, 103, 104, and 106-109 claim the use of *SgfI*, *PmeI*, and/or *PacI*, all rare cutter endonucleases that recognize 8 bp restriction sites. The designation and use of these enzymes as infrequent cutters, therefore, is unequivocally outside the disclosure of Parrott. The cited references thus fail to teach or suggest every element of claims 6, 7, 9, 89-92, 103, 104, and 106-109, and allowance of these claims is respectfully requested.

CONCLUSION

In view of the foregoing, applicants respectfully request allowance of the pending claims. In addition, the pending claims may contain subject matter that is allowable for additional reasons not discussed herein. Should any questions remain, the Examiner is encouraged to contact the undersigned at 608.257.3501.

Respectfully submitted,

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